## REMARKS

Claims 1-10, 12-16, 21, 22, 26, 27, 29-32, 50-87, 89-97, and 101-119 are now pending in the case, claims 28 and 88 having been cancelled by the above amendment. Claims 1 and 2 have been amended to replace the term "additives" with "excipients", a limitation that is supported, for example, at page 2, lines 27-31 of the specification. Claims 21 and 78 are amended to depend from claim 1. Since claims 59 and 94 cover the bile salt embodiment, this embodiment has been deleted from claims 56 and 89 as unnecessarily redundant. The remaining amendments are to ensure all of the dependent claims are consistent with the claims from which they depend. No new matter has been added. Attached is a marked-up version of the changes being made by the current amendment.

The Office Action mailed December 28, 2001, indicates that claims 1, 3-10, 12-16, 31, 101, 102, 103-118 are, to the extent that they have been examined, characterized as allowable. Applicants point out that claim 119, added with the amendment filed on October 4, 2001, was not addressed by the present Office Action. As it depends from allowable claim 102, acknowledgement that claim 119 is also allowable is respectfully requested.

In the telephonic interview with the undersigned on February 7, 2002, the Examiner said that claim 1 would be allowable if part (C) were deleted from the claim or amended to exclude the possibility that the "additive" is an active ingredient that does not meet the diameter limitation applied to parts (A) and (B). Applicants have accordingly replaced the term "additive" with "excipient" to exclude this possibility. All other claims that referred to "additive" are similarly amended for consistency. According to Dorland's Illustrated Medical Dictionary, 27th Edition, an "excipient" is "any more or less inert substance added to a prescription in order to confer a suitable consistency or form to the drug." As this excludes active ingredients, this should allay the Examiner's concerns about part (C) of claim 1.

As suggested by the Examiner in the telephonic interview, Applicants have amended claim 21 (drawn to a method) and claim 78 (drawn to a dry powder inhaler device) to depend from, and thereby have the same scope as, claim 1. The Examiner said that if this were done, he

would rejoin the method and device claims with the case. Thus, rejoinder and allowance of claims 21-27, 29, 30, 50-60, 78-87, and 89-97 is respectfully requested.

On page 4 of the Office Action, the Examiner notes that reference "AR" (Kohler, 1987) was stricken from the IDS because of the absence of a translation. Applicants enclose a new translated version of the Kohler 1987 reference, and ask that it be considered and the enclosed new Form 1449 be initialed accordingly.

Applicants ask that all claims be allowed. Enclosed is a Petition for Extension of Time and a $110 check for the applicable fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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**Version with markings to show changes made**

In the claims:

Claims 28 and 88 have been cancelled.

Claims 1, 2, 21, 29, 30, 56, 59, 78, 89, 90, 93, 94, and 96 have been amended as follows:

1. (Thrice Amended) A propellant-free composition consisting of (A) a polypeptide, (B) one or more surfactant compounds which (i) have a consistency that permits them to be processed into primary particles having a diameter less than 10 microns, and (ii) enhance the systemic absorption of said polypeptide in the lower respiratory tract of a patient, and (C) optionally one or more non-hygroscopic [additives] excipients, said composition being in the form of a dry powder suitable for inhalation from a dry powder inhaler device, wherein at least 50% of the total mass of (A) and (B) consists of primary particles having a diameter less than 10 microns or equal to about 10 microns, and wherein each of the one or more surfactant compounds is selected from the group consisting of a salt of a fatty acid, bile salt, single-chain phospholipid, double-chain phospholipid in which each chain of the double-chain phospholipid is eight or fewer carbon atoms in length, alkyl glycoside, cyclodextrin or derivative thereof, salt of a glycyrrhizine acid, salt of a saponin glycoside, salt of an acyl carnitine, and sodium salicylate.

2. (Amended) A composition as claimed in claim 1, including said one or more non-hygroscopic [additives] excipents, said one or more non-hygroscopic [additives] excipents comprising a carrier that comprises either

(a) particles having a diameter of less than 10 microns or equal to about 10 microns, such that at least 50% of said composition consists of primary particles having a diameter of less than 10 microns or equal to about 10 microns; or

(b) coarse particles having a diameter of at least 20 microns, such that an ordered mixture is formed between (i) the carrier and (ii) the polypeptide of (A) and the one or more surfactant compounds of (B).

21. (Amended) A method for systemic administration of a biologically active polypeptide, comprising

providing [a composition comprising a mixture of active compounds (A) a biologically active polypeptide, and (B) an enhancer compound which (i) has a consistency that permits it to be processed into primary particles having a diameter less than 10 microns, and (ii) enhances the systemic absorption of the polypeptide in the lower respiratory tract of a patient, said composition being in the form of a dry powder suitable for inhalation from a dry powder inhaler device] composition of claim 1 ; and

causing said patient to inhale [through the mouth] said composition from a dry powder inhaler device[; provided that at least 50% of the total mass of the active compounds, at the point the active compounds enter the respiratory tract of the patient, consists of particles having a diameter less than 10 microns or equal to about 10 microns].

29. (Amended) The method of claim [28] 21 wherein the [enhancer] surfactant compound is a salt of a fatty acid.

30. (Amended) The method of claim 29 wherein the [enhancer] surfacant compound is sodium caprate.

56. (Amended) The method of claim [28] 21, wherein said surfactant compound is [a bile salt,] a bile salt derivative, an alkyl glycoside, a cyclodextrin or derivative thereof, or a phospholipid.

59. (Amended) The method of claim 21, wherein said [enhancer] surfacant compound is a bile salt.

78. (Amended) A dry powder inhaler device containing [a composition comprising a mixture of active compounds (A) a biologically active polypeptide, and (B) an enhancer compound which (i) has a consistency that permits it to be processed into primary particles

having a diameter less than 10 microns, and (ii) enhances the systemic absorption of said polypeptide in the lower respiratory tract of a patient, said composition being in the form of a dry powder suitable for inhalation from a dry powder inhaler device, wherein at least 50% of the total mass of active compounds consists of primary particles having a diameter less than 10 microns or equal to about 10 microns, said primary particles optionally being formed into agglomerates; the dry powder inhaler device being adapted for inhalation through the mouth] the composition of claim 1.

89. (Amended) The dry powder inhaler device of claim [88] 78, wherein said surfactant compound is [a bile salt,] a bile salt derivative, an alkyl glycoside, a cyclodextrin or derivative thereof, or a phospholipid.

90. (Amended) The dry powder inhaler device of claim [88] 78, wherein said surfactant compound is a salt of a fatty acid.

93. (Amended) The dry powder inhaler device of claim [88] 78, wherein said surfactant compound is sodium caprate.

94. (Amended) The dry powder inhaler device of claim 78, wherein said [enhancer] surfacant compound is a bile salt.

96. (Amended) The dry powder inhaler device of claim 78, wherein said [composition is in the form of said] primary particles are formed into agglomerates, said device being configured to induce the majority of said agglomerates to break down into particles having a diameter less than 10 microns or equal to about 10 microns, upon inhalation of said agglomerates from said device.